



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

November 21, 2001

MEMORANDUM

Subject: Acute Toxicity Review for EPA File Symbol: 72674-EA / Densil DG
DP Barcode: D277594
Case No: 070296

To: Marshall Swindell, PM 33 / Martha Terry
Regulatory Management Branch
Antimicrobials Division (7510C)

From: Ian Blackwell, Biologist
Efficacy Evaluation Team
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ILB 11/29/01

Through: Karen Hicks, Team Leader
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K.Hicks 11/29/01

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Applicant: Avecia, Inc.

FORMULATION FROM LABEL:

Active Ingredient(s):
N-Butyl-1,2-benzisothiazolin-3-one
Other Ingredient(s):

% by wt.

45

55

Total:

100%

BACKGROUND: Avecia, Inc., has submitted a response to a 7/16/2001 PSB/AD review of their product, "Densil DG". In that review, the registrant was asked to:

- Identify the test material DS 6039 and its relationship to Densil DG.
- Address the missing acute inhalation toxicity study.
- Address the missing primary eye irritation study.

An August 8, 2001, letter from Avecia states that they request a waiver of the primary irritation study based upon the results of the primary skin irritation study. This letter also states that the registrant has submitted MRID Number 450830-04 for the acute inhalation toxicity study. The registrant states that "DS 6039" is indeed Densil DG Fungicide.

RECOMMENDATIONS: PSB findings are:

1. The acute oral toxicity, acute dermal toxicity, primary skin irritation and dermal sensitization studies are identified as having been conducted on Densil DG and are now acceptable.
2. The acute inhalation toxicity study is not acceptable and must be reconducted. The problem with this study is that it did not determine an acute toxicity category. The test results indicating that the LC_{50} is between 0.197 and 0.733 mg/L do not allow this study to be placed into a toxicity category.
3. The primary eye irritation study is waived based upon the results of the primary skin irritation study and is assigned toxicity category I.

The acute toxicity profile for File Symbol 72674-EA is currently:

acute oral toxicity	III	acceptable
acute dermal toxicity	III	acceptable
acute inhalation toxicity		unacceptable
primary eye irritation	I	waived
primary skin irritation	I	acceptable
dermal sensitization	Sensitizer	acceptable

LABELING:

NOTE: This product labeling may change upon the receipt and review of an acute toxicity study conducted on 72674-EA.

SIGNAL WORD: DANGER

Hazards to Humans and Domestic Animals:

Restricted Use Pesticide due to toxicity categories. For retail sale to and use only by Certified Applicators or persons under their direct supervision, and, only those used covered by the Certified Applicator's certification.

Corrosive. Causes irreversible eye damage and skin burns. Harmful if swallowed. Harmful if absorbed through skin. Do not get in eyes, on skin, or on clothing. Wear: Coveralls worn over long-sleeved shirt and long pants. Socks. Chemical-resistant footwear. Gloves. Protective eyewear. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Remove and wash contaminated clothing before reuse. Avoid contact with skin, eyes or clothing. Wear: Long-Sleeved shirt and long pants. Shoes.

Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals.

First Aid:

If in eyes:

- Hold eye open and rinse slowly and gently with water for 15-20 minutes.
- Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
- Call a Poison Control Center or doctor for treatment advice.

If Swallowed:

- Call a Poison Control Center or doctor immediately for treatment advice.
- Have the person sip a glass of water if able to do so.
- Do not induce vomiting unless told to by a poison control center or doctor.
- Do not give anything to an unconscious person.

If on skin:

- Take off contaminated clothing.
- Rinse immediately with plenty of water for 15-20 minutes.
- Call a poison control center or doctor for treatment advice.
- Have the product container or label with you when calling a poison control center or doctor, or when going for treatment.

Note to Physician: Probably mucosal damage may contraindicate the use of gastric lavage.

DATA REVIEW FOR ACUTE INHALATION TOXICITY (§81-3, 870.1300)

Product Manager: 33
MRID No.: 450830-04

Reviewer: I. Blackwell
Study Completion Date: 9/10/97
Report No.: CTL/P/5556

Testing Laboratory: Central Toxicology Laboratory, Alderly Park
Author: N. J. Rattay

Quality Assurance (40 CFR §160.12): Included

Test Material: DS 6039; Densil 6039, "brown liquid"
Concentration: $0.193 < X < 0.733$ mg/L, nose-only exposure

Species: rat, Plk: AP,SD
Weight: males= 298-372 g; females = 222-243 g
Age: 8-12 weeks (young adult)
Source: Zeneca Rodent Breeding Unit

Summary:

1. LC_{50} (mg/L): Males =
 Females =
 Combined =

2. The estimated LC_{50} is

3. MMAD: see Table 2

4. Tox. Category:

Classification: Unacceptable

Procedure (Deviation From §81-3):

The results do not allow the determination of a toxicity category for this study.

Results:

Reported Mortality

Exposure Concentration	(NUMBER DEATHS/NUMBER TESTED)		
	Males	Females	Combined
0.197 mg/L	0/5	0/5	0/10
0.733 mg/L	2/5	1/5	3/10

Chamber Atmosphere		
Dose Level	MMAD	GSD
0.197 mg/L	1.765 μm	2.105 μm
0.733 mg/L	1.450 μm	3.290 μm

Chamber Environment	
Chamber Volume	27.6 liters
Airflow	37 lpm
Temperature	22 ° C
Relative Humidity	30-70%

Clinical Observations: Labored breathing, reduced breathing, gasping, salivation, piloerection, splayed gait, runny nose, chromodacryorrhea, test substance stains around snout.

Gross Necropsy Findings: G.I tract distended with gas, stained mouth, lungs dark and/or mottled.